

AMENDMENTS TO THE CLAIMS

1. **(Currently Amended)** A method for attenuating expression of an endogenous genomic target gene in mammalian cells, comprising introducing into mammalian cells suspended in culture an expression vector encoding a hairpin RNA which, when transcribed from said expression vector in said mammalian cells, attenuates expression of the endogenous target-gene, wherein the transcribed hairpin RNA:

(i) is a single nucleic acid strand having a double stranded portion including first nucleotide sequence that hybridizes under stringent wash conditions of 0.2 x SSC at 65 °C to a portion of the endogenous target-gene of the mammalian cell, and a second nucleotide sequence which is a complementary inverted repeat of said first nucleotide sequence and hybridizes to said first nucleotide sequence to form a hairpin structure;

(ii) is a substrate for cleavage by an RNaseIII enzyme to produce a double-stranded RNA product,

(iii) does not produce a general sequence-independent killing of the mammalian cells, and

(iv) reduces expression of said endogenous target-gene in a manner dependent on the sequence of said double stranded portion of the hairpin RNA.

2-8. **(Canceled)**

9. **(Canceled)**

10. **(Canceled)**

11. **(Canceled)**

12. **(Previously presented)** The method of claim 1, wherein the mammalian cells are primate cells.

13. **(Canceled)**

14. **(Previously presented)** The method of claim 12, wherein the mammalian cells are human cells.

15. **(Currently Amended)** The method of claim 1, wherein expression of the endogenous target gene is attenuated by at least 5 fold compared to the expression of the endogenous gene in mammalian cells suspended in culture into which an expression vector encoding the hairpin RNA has not been introduced.
- 16-27. **(Canceled)**
28. **(Previously presented)** The method of claim 1, wherein the hairpin RNA does not cause activation of a protein kinase RNA-activated (PKR) sequence-independent response in the mammalian cells.
- 29-46. **(Canceled)**
47. **(Previously presented)** The method of claim 1, wherein the RNaseIII enzyme is dicer.
48. **(Currently Amended)** A method for attenuating expression of a endogenous genomic target gene in mammalian cells, comprising introducing into mammalian cells suspended in culture an expression vector encoding a hairpin RNA which, when transcribed from said expression vector in said mammalian cells, attenuates expression of the endogenous target-gene, wherein the transcribed hairpin RNA:
- (i) is a single nucleic acid strand having a double stranded portion including first nucleotide sequence of the endogenous target-gene, and a second nucleotide sequence which is a complementary inverted repeat of said first nucleotide sequence and hybridizes to said first nucleotide sequence to form a hairpin structure;
 - (ii) is a substrate for cleavage by an RNaseIII enzyme to produce a double-stranded RNA product,
 - (iii) does not produce a general sequence-independent killing of the mammalian cells, and
 - (iv) reduces expression of said endogenous target-gene in a manner dependent on the sequence of said double stranded portion of the hairpin RNA.

49. (New) The method of any of claims 1, 12, 14, 15, 28, 47 or 48, wherein the double stranded portion of the transcribed hairpin RNA is 20 to 50 base pairs in length.

50. (New) The method of any of claims 1, 12, 14, 15, 28, 47 or 48, wherein the RNaseIII enzyme is Dicer.